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10/781,014	02/17/2004	Markus Pompejus	BGI-126CPCN	2283

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EXAMINER	
FRONDA, CHRISTIAN L	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 01/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/781,014	POMPEJUS ET AL.	
	Examiner	Art Unit	
	Christian L. Fronda	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *39-59* is/are pending in the application.

4a) Of the above claim(s) *47-59* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restriction

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 39-46, drawn to an isolated nucleic acid molecule, vector, host cell, and method for making a polypeptide, classified in class 435, subclass 69.1.

II. Claim 47-53, drawn to a method for making a fine chemical, classified in class 435, subclass 41.

III. Claims 54-56, drawn to an isolated polypeptide, classified in class 530, subclass 350.

IV. Claim 57, drawn to a method for diagnosing the presence or activity of *Corynebacterium diphtheriae* in a subject comprising detecting the presence of at least one nucleic acid molecule, classified in class 435, subclass 6.

V. Claim 58, drawn to a method for diagnosing the presence or activity of *Corynebacterium diphtheriae* in a subject comprising detecting the presence of at least one polypeptide, classified in class 435, subclass 7.1.

VI. Claim 59, drawn to a host cell comprising a nucleic acid molecule that is disrupted, classified in class 435, subclass 252.3.

2. The inventions are distinct, each from the other because of the following reasons:

Inventions of Group I, III, and VI are patentably distinct products because each of the products of Groups I, III, and VI are independent chemical entities that require different literature searches. Polypeptides, which are composed of amino acids, and polynucleotides, which are composed of purine and pyrimidine units, are structurally distinct molecules. Furthermore, the nucleic acid molecule within the host cell of Group VI is independent and patentably distinct from the nucleic acid molecule of Group I since they have different nucleotide sequences and structures which require different literature searches.

Inventions of Groups II, IV, and VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of

operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). The processes of Groups II, IV, and VI are distinct both physically and functionally; require different process steps, reagents, and parameters; have different purposes; and produce different products.

Inventions of Groups II-IV and VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). Each of the processes of Groups II and IV do not require the products of Group III and VI.

Inventions of Groups I, V, and VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). The process of Group V does not require the products of Group I and VI.

Inventions of Group I and Groups (II and IV) are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product as claimed can be used in a materially different process of using that product such as using the nucleic acid molecule in a process for the recombinant production of a polypeptide.

Inventions of Group III and Group V are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product as claimed can be used in a materially different process of using that product such as using the polypeptide in a process for producing antibodies against the polypeptide.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

3. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by

37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of In re Ochiai, In re Brouwer and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

4. During a telephone conversation with Maria Laccotripe Zacharakis on 01/04/2006, a provisional election was made without traverse to prosecute the invention of Group I, claims 39-46. Affirmation of this election must be made by applicant in replying to this Office action. Claims 47-59 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

5. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(I).

6. Acknowledgment is made of applicant's claim for foreign priority based on 27 applications filed in Germany in 1999. It is noted, however, that applicant has not filed a certified copy of the 27 applications as required by 35 U.S.C. 119(b).

Claim Rejections - 35 U.S.C. § 112, 2nd Paragraph

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 39-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 39, the phrase "set forth" renders the claim vague and indefinite because it is unclear if applicants are actually referring to the specific SEQ ID NOs. Claims 40-46 which depend from claim 39 are also rejected because they do not correct the defect of claim 39. Amending the claim to recite "the nucleotide sequence of SEQ ID NO: 179" and "the amino acid sequence of SEQ ID NO: 180" may overcome this rejection.

In claim 29, the phrase "a complement thereof" renders the claim vague and indefinite because it is unclear if applicants are actually referring to a nucleotide sequence that is the full and complete complement of SEQ ID NO: 179 or a complement of a part of SEQ ID NO: 179. Amending the claim to recite "the complement of SEQ ID NO: 179" may overcome the rejection

Claim Rejections - 35 U.S.C. § 112, 1st Paragraph

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 39-46 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid comprising the nucleotide sequence SEQ ID NO: 179 and an isolated nucleic acid encoding the amino acid sequence SEQ ID NO: 180; does not reasonably provide enablement for any nucleic acid molecule comprising a nucleotide sequence which is at least 50% identical to SEQ ID NO: 179 or a complement thereof, any nucleic acid molecule which encodes any naturally occurring allelic variant of a polypeptide comprising SEQ ID NO: 180, and any isolated nucleic molecule comprising a fragment of at least 15 contiguous

nucleotides of SEQ ID NO: 179. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized In re Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of the claim 38 encompasses any nucleic acid molecule comprising a nucleotide sequence which is at least 50% identical to SEQ ID NO: 179 or a complement thereof, any nucleic acid molecule which encodes any naturally occurring allelic variant of a polypeptide comprising SEQ ID NO: 180, and any isolated nucleic molecule comprising a fragment of at least 15 contiguous nucleotides of SEQ ID NO: 179. The specification provides guidance and examples for a nucleic acid molecule consisting of the nucleotide sequence of SEQ ID NO: 179 which encodes a phosphoenolpyruvate carboxykinase from *Corynebacterium glutamicum* consisting of the amino acid sequence of SEQ ID NO: 180. The specification discloses that SEQ ID NO: 179 consists of 1953 nucleotides and SEQ ID NO: 180 consists of 610 amino acid residues. However, the specification does not provide guidance, prediction, and working examples for making any nucleic acid molecule comprising a nucleotide sequence which is at least 50% identical to SEQ ID NO: 179 or a complement thereof and any nucleic acid molecule which encodes any naturally occurring allelic variant of a polypeptide comprising SEQ ID NO: 180. Furthermore, the specification does not provide guidance, prediction, and working examples for making and/or using any isolated nucleic molecule comprising a fragment of at least 15 contiguous nucleotides of SEQ ID NO: 179

Thus, an undue amount of trial and error experimentation must be preformed to make the claimed nucleic acids. Such experimentation entails searching and screening for 977 specific nucleotides in SEQ ID NO: 179 to change using nucleotide substitution, insertion, deletion, addition, and combinations thereof, and then determining whether the polynucleotide can encode any functional phosphoenolpyruvate carboxykinase. Experimentation also entails searching and screening vast number of biological sources for any naturally occurring allelic variant of SEQ ID NO: 180 and then obtaining the nucleic acid encoding the variant. Furthermore, experimentation involves selecting any 15 contiguous nucleotides of SEQ ID NO: 179 and determining the biological function and use of the selected 15 contiguous nucleotides of SEQ ID NO: 179. General teaching regarding screening and searching for the claimed invention using phosphoenolpyruvate carboxykinase assays taught in the specification is not guidance for making

the claimed invention.

In view of the above considerations, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claims. Claims 40-46 which depend from claim 39 are also rejected because they do not correct the defect of claim 39.

11. Claim 43 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether undue experimentation is required, are summarized In re Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of the claims encompass transgenic plants and animals including humans transformed with the claimed vector, where the vector comprises the nucleic acid molecule of claim 39.

While the specification provides guidance for transforming isolated *E.coli* host cells with the vector, the specification does not provide guidance, prediction, and working examples for making transgenic plants and animals including humans transformed with the claimed vector. Thus, an undue amount of trial and error experimentation must be preformed to make the claimed transgenic plants and animals including humans and determining whether the claimed vector expresses the claimed nucleic acid molecules.

In view of the above considerations, the specification does not enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the transgenic plants and animals including humans transformed with the claimed vector

12. Claims 39-46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 39 is drawn to a genus of complements of SEQ ID NO: 179, a genus of

complements of any nucleic acid molecule encoding SEQ ID NO: 180, a genus of nucleic acid molecules encoding naturally occurring allelic variants of a polypeptide comprising SEQ ID NO: 180, a genus of nucleic acid molecules that is at least 50% identical to SEQ ID NO: 179, and a genus of nucleic acid molecules comprising any fragment of at least 15 contiguous nucleotides of SEQ ID NO: 179. The scope of the each genus includes many members with widely differing structural, chemical, and physiochemical properties including widely differing nucleotide sequences. Furthermore, each genus is highly variable because a significant number of structural differences between genus members exists.

While the specification discloses a nucleic acid molecule consisting of the nucleotide sequence of SEQ ID NO: 179 which encodes a phosphoenolpyruvate carboxykinase from *Corynebacterium glutamicum* consisting of the amino acid sequence of SEQ ID NO: 180; there is no recitation of any particular structure to function relationship in the claims which would define any biological properties and enzyme activities common to the members of each genus. Furthermore, the specification does not define any structure to function relationship for each claimed genus other than the polynucleotide of SEQ ID NO: 179 encoding a phosphoenolpyruvate carboxykinase consisting of the amino acid sequence of SEQ ID NO: 180. Thus, one skilled in the art cannot visualize or recognize the identity of the members of each genus.

In regard to the claimed genus of nucleic acid molecules encoding naturally occurring allelic variants of SEQ ID NO: 180, the nature of alleleic variants is that they are variant structures where the structure and function of one does not provide guidance to the structure and function of others. Although the specification discloses only one allele within the scope of the genus which is SEQ ID NO:179, the general knowledge in the art concerning alleles as exemplified by Rieger et al., (Glossary of Genetics (1991), p. 16) is that there is no any indication of how the structure of one allele is representative of other unknown alleles having concordant or discordant functions. One of skill in the art would conclude that applicants were not in possession of the claimed genus because a description of only one member of this genus is not representative of the variants of the genus and is insufficient to adequately describe the claimed genus of nucleic acid molecules encoding naturally occurring allelic variants of a polypeptide comprising SEQ ID NO: 180.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definitions, such as the structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v, Eli Lilly and Co.* 43 USPQ2d 1398 (Fed. Cir. 1997), quoting *Fiers v. Revel*, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe the genus of

genetic materials, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g. structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these. Therefore, the instant claims are not adequately described.

In view of the above considerations, one of skill in the art would not recognize that applicants were in possession of a genus complements of SEQ ID NO: 179, a genus complements of any nucleic acid molecule encoding SEQ ID NO: 180, a genus of nucleic acid molecules encoding naturally occurring allelic variants of a polypeptide comprising SEQ ID NO: 180, a genus of nucleic acid molecules that is at least 50% identical to SEQ ID NO: 179, and a genus of nucleic acid molecules comprising any fragment of at least 15 contiguous nucleotides of SEQ ID NO: 179. Claims 40-46 which depend from claim 39 are also rejected because they do not correct the defect of claim 39.

Amending the claims to recite that the claimed isolated nucleic acid molecule encodes a phosphoenolpyruvate carboxykinase may overcome the rejection.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

14. Claims 39 is rejected under 35 U.S.C. 102(e) as being anticipated by Fleischman et al. (US Patent 6,294,328).

Fleischman et al. (US Patent 6,294,328) teach an isolated nucleic acid molecule encoding an amino acid sequence that is 65% identical to SEQ ID NO: 180 (see attached alignment).

Because claim 1 does not specifically state a biological function and specifically state that the encoded naturally occurring alleleic variant must have 100% amino acid identity to SEQ ID NO: 180, than the examiner takes the position that the teachings of Fleischman et al. anticipate the claim.

15. Claims 39, 41-44 and 46 are rejected under 35 U.S.C. 102(b) as being anticipated by Abrams et al. (US Patent 5,604,116).

Abrams et al. teach an isolated nucleic acid molecule that comprises 18 consecutive nucleotides of SEQ ID NO: 179 (see attached alignment), vectors and host cells comprising said isolated nucleic acid molecule, and a method for expressing said nucleic acid molecule in a host cell such as *E.coli* to produce a polypeptide (see entire patent especially Abstract; claims; and column 2, line 19 to column 28, line 56). Thus, the reference teachings anticipate the claimed invention.

Conclusion

16. No claim is allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L Fronda whose telephone number is (571)272-0929. The examiner can normally be reached Monday-Friday between 9:00AM - 5:00PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura N Achutamurthy can be reached on (571)272-0928. The fax phone number for the organization where this application or proceeding is assigned is (571)273-8300.

18. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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